Neurotech *Guide book*

Where is Neurotech today?

2023/06/23 v1.3

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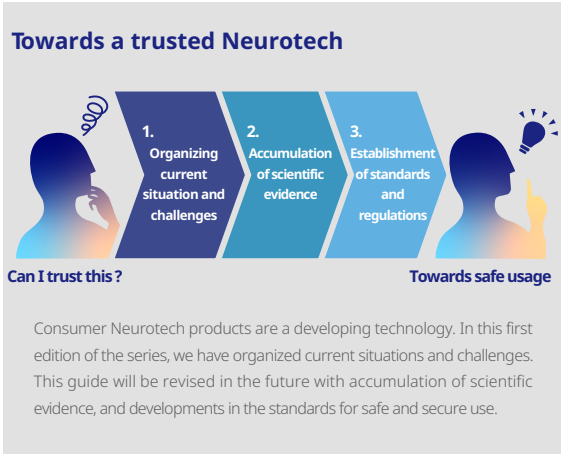
This guidebook was produced as part of the "Liberation from Biological Limitations via Physical, Cognitive and Perceptual Augmentation (Project Manager Ryota Kanai)" project for Goal 1 of the Cabinet Office Moonshot Research and Development Program, "Overcoming limitations of body, brain, space and time" by 2050.

Preface

This guidebook is written for those interested in the current situation and challenges around Neurotech products. In recent years, "Neurotechnology" or so-called "Neurotech", which is the technology that aims to estimate and regulate the state of the human brain, is spreading rapidly. When you search the Internet or social media, you will find many Neurotech products for general consumers. Brochures for such products make enticing claims such as "improved concentration," "improved sleep," or "improved athletic performance". However, is there any scientific basis for these claims? Are there any dangers in ordinary consumers using such products on their own?

Neurotech is a developing technology whose efficacy and safety have not yet been fully clarified. Because it works on the brain itself, a specialized organ that controls thought and personality, it is necessary to consider not only safety but also ethical, social, and legal issues. However, no official standards exist yet to address these issues. Consumers must be cautious when purchasing and using products, recognizing that there are still unknown and unresolved issues. Neurotech businesses must also develop trusted products and services while confronting these realities.



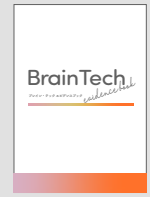
Consumer Neurotech products are a developing technology. In this first edition of the series, we have organized current situations and challenges. This guide will be revised in the future with accumulation of scientific evidence, and developments in the standards for safe and secure use.

Given this situation, Neurotech is not something that we can recommend to the general public yet. Therefore, we published this guidebook to accurately share the current situation and challenges around Neurotech with you. We hope that this guidebook will be helpful to consumers and businesses by providing basic information about Neurotech, the risks and challenges associated with its use, and considerations when selecting and developing products and services. This document was compiled based mainly on research conducted on healthy adults. Minors and Neurotechs for medical purposes such as diagnosing and treating diseases are not the subject of this guidebook, and therefore not addressed. For product intended as medical devices (medical/research-grade Neurotech products), please refer to the information published by related academic societies and industry associations.

This guidebook was developed by a Guidebook Development Committee consisting of experts from universities, research institutions, and private companies. Basic questions such as "What is Neurotech?" and "What should I be aware with regards to commercial products?" were set as General Questions (GQ), and answers were compiled based on the scientific knowledge and opinions gathered by the committee members.

This guidebook was originally published in Japanese as a part of the Moonshot R&D program "Liberation from Biological Limitations via Physical, Cognitive and Perceptual Augmentation."[1] The English version of the guidebook is intended to inform the international community about the current situation and challenges around Neurotech. We hope that this guidebook will deepen your understanding of Neurotech and that it will develop as a safe and secure technology.

【Guidebook】
- For those who are interested in Neurotech products
- Created by a committee of researchers, physicians, and industry persons who are knowledgeable in neuroscience
- Provides correct knowledge and perspectives that are currently available, as well as information on how to approach Neurotech



【Evidence Book】
- For Neurotech users and providers of products and services
- Created by an evidence evaluation committee consisting of researchers specializing in neuroscience
- Summarizes the effectiveness and safety of Neurotech based on the results of systematic reviews

Apart from this, we are developing an "Evidence Book" that summarizes evidence related to Neurotech, under an Evidence Evaluation Committee composed of several researchers specializing in neuroscience. The Evidence Evaluation Committee is answering the question of how much scientific evidence there are for the claims made by Neurotech products through the scientific method of systematic review. Some results of this analysis will be available in July 2023.

By Neurotech Guidebook Development Committee

Preface

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Disclaimer: Please read carefully

The authors of this guidebook have carefully checked that the matters and analysis described are accurate, and furthermore, its contents have been verified by an external review board composed by experts in the fields of medicine and medical ethics, and revised after receiving feedback from relevant academic societies and legal experts. However, the accuracy of the content cannot be completely guaranteed due to a number of uncertain factors, including future technological developments, the uniqueness of targeting the brain, changes in views due to the accumulation of research and social circumstances, differences in views depending on one's positions, differences in physical characteristics and usage conditions of the consumers, characteristics of the products, and revisions to the legal system. Therefore, we assume no responsibility for any health hazards or legal issues that may arise in reference to this guidebook. In addition, please do not refer to this guidebook with regards to Neurotech intended for minors or medical care, such as the diagnosis or treatment of illnesses, as they are outside the scope of this guidebook.

GQ1 What is Neurotech/BMI?

Summary

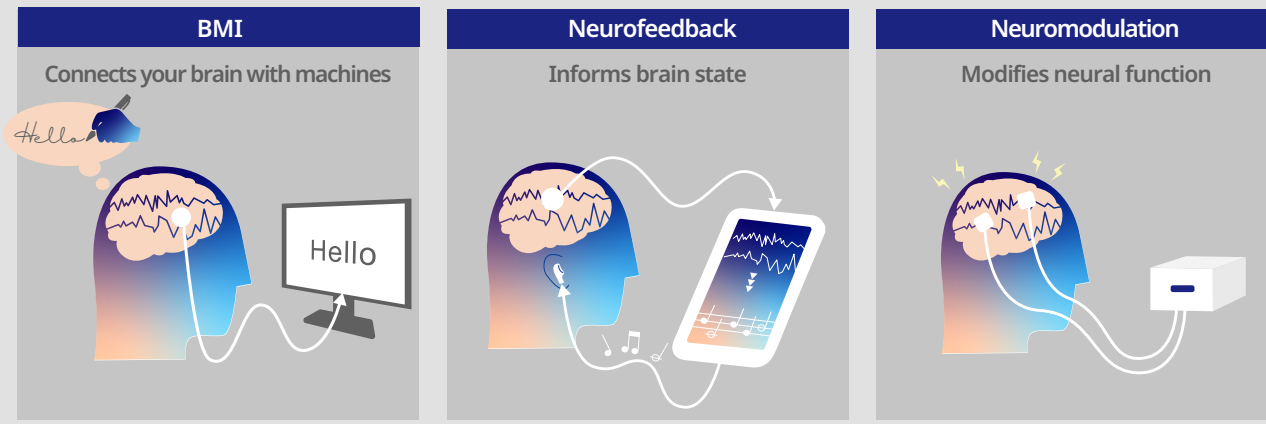
Neurotech is a term that combines the words "neuro-" (relating to nerves or the nervous system) and "technology", and refers to products, systems, and services developed by integrating knowledge and techniques in neuroscience and engineering. It is also called Brain-Machine Interface (BMI) or Brain-Computer Interface (BCI) in the sense of technology that connects the brain and machinery (machines and computers). By measuring brain activity and estimating human intentions and conditions, it is possible to control machines or, conversely, to send stimulation to the brain from machines. These are also applied in technologies that aim to modulate brain functions, such as neurofeedback and neuromodulation.

Explanation

Neurotech is a term that combines the words "neuro-" (relating to nerves or the nervous system) and "technology" and is also called "Neurotechnology". It is sometimes called BMI or BCI, with the focus on the interface technology that connects the brain and machines. There is no clear distinction between BMI and BCI.

In the Neurotech market, it is often referred to as BMI when the purpose is operating a machine. When we take action, we first think, decide what to do, and send commands to move our bodies with our brains. BMI measures the brain signals (brain activity) in that thinking state, estimates the intention, and transmits it to the machine. As a result, successfully reading and processing brain signals allows for the machine to be moved without physically moving. For example, people who are physically immobile because of illness or injury can now operate machines with BMI to supplement their physical functions, such as inputting text to convey their intentions, or moving robots. Additionally, BMI products have also been developed for entertainment purposes, such as controlling toys and drones, as well as avatars in games (Table1). Other applications of these technologies include neurofeedback (GQ2), which adjusts brain states, and neuromodulation (GQ3), which stimulates the brain to regulate brain function.

Neurotech Examples



What is Neurotech?

Neurotech includes products such as BMI, which connects the brain to machinery (machines and computers), neurofeedback, which uses this technology to inform about the brain's condition, and neuromodulation, which stimulates the brain. The time may come when Neurotech products will be accessible in a form similar to "health devices" . But what kind of effects will we actually feel? Will there be any negative effects on the brain or body? Will others be able to read our thoughts and misuse them? These are the current state of various expectations and anxieties.

GQ2

What is neurofeedback?

Summary

Neurofeedback is a technology that measures brain activity and communicates it to the user through images, sounds, or even touch, taste, and smell of the five senses. It is expected to enable users to easily understand their own brain activity and to train themselves to adjust the magnitude of their brain activity. Among Neurotech products for general consumers, those that claim to improve concentration and to promote relaxation fall into this category, and a variety of benefits have been claimed. However, it is important to note that more than a few of these products have not been adequately tested for efficacy and safety.

Explanation

What types of neurofeedback products for general consumers are available?

According to a survey[2] by NTT DATA Management Consulting, the main applications advocated by BMI and neurofeedback products for general consumers were categorized into healthcare, capability enhancement, fundamental technology for IOT, marketing, entertainment, and education (as of 2022). Of these, neurofeedback is about to be used for healthcare and capability enhancement usages (Table1). For example, it is said that by measuring the brain waves of users and outputting images and sounds based on those brain waves, users can train themselves to change their own brain waves using the images and sounds as cues. The products are sold and marketed with the expectation that this will improve concentration and relaxation. However, the reality is that these claims are only made by sellers on their websites or in their product catalogs, and their effectiveness has not been sufficiently verified.

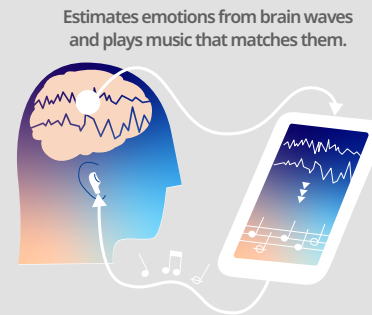
Domain	Examples	Domain	Examples
Healthcare	Stress and anxiety relief / Improving sleep quality / Support for mindfulness and meditation / Assessment of cognitive function / Assessment of concussion / Relief of eye strain / Pain relief / Assist in psychotherapy / Fatigue detection	Fundamental Technologies for IoT	Application to online platforms / Application to API systems / BMI to operate devices and communicate intentions
Enhancement of Ability	Improving concentration / Improving learning skill / Improving memory function / Improving sports performance	Marketing	Emotional estimation / Design evaluation
		Entertainment	Avatar control / Telepathic games / Communication tools / Music playback
		Education	Support for monitoring and improving concentration

Table 1. Areas of BMI and neurofeedback products marketed to the public and the effects they advocate.

Caution: The above product examples are only one-sided claims made by the sellers on their websites or in their product catalogs. Whether the efficacy and safety of the products have been scientifically proven was not verified by this Guidebook. In addition, most of the products are sold overseas and have gone through a translation process into Japanese, but if such efficacy claims are made, they may contain products that, according to the law and regulations, should be manufactured and sold as medical devices in Japan. Please thoroughly check the relevant laws and regulations when selling products.

An Example of Neurofeedback

For example, in the figure on the right, brain signals are measured by an electroencephalograph and processed on a computer to estimate the "sadness" that person is feeling. Depending on the estimated degree of "sadness," music in a sad mood is played (feedback). As a result, when you listen to the music played, you become aware of your own emotional state . By further adjusting one's own brain activity and by trying to hear more "pleasant" music (training), one acquires the skill of self-regulating one's own brain activity. As in the above example, "through sounds and other means, perceiving (feedback of)" one's "own brain activity (neuro)" is called neurofeedback.



Are consumer-grade neurofeedback products safe?

The safety of consumer neurofeedback products has not been fully tested, and it is unclear what risks are associated with the use of consumer neurofeedback products in everyday life. A report published in 2020 on the side effects of using medical/research-grade products reported the occurrence of side effects in 5 out of 21 experiments that used neurofeedback[3]. The most commonly occurring side effects were headset discomfort and drowsiness, followed by irritation and headache[3]. Another report in 2015 also identified side effects such as decline in performance and sleep disturbances[4]. However, these reports include people with medical conditions and may not be directly applicable to healthy adults (Table 2). We also do not know if cases of particular products can be applicable to neurofeedback technology in general. There are other precautions to keep in mind with brain interventions themselves, as discussed in Appendix 2, "Risks and Ethical Issues Associated with the Use of Neuro Technology".

Thus, there are still unknown risks and unresolved issues with neurofeedback. When using consumer neurofeedback products, be aware of these uncertainties and use them with caution. If symptoms of concern appear, stop using the product immediately and consult a healthcare provider. Depending on the symptoms, we also recommend reporting to the National Consumer Center (see Note 1). However, even if side effects do occur, if the product is not an approved medical device, the Relief Systems for Adverse Drug Reactions (see Note 2) does not apply. In other words, please keep in mind that the use of consumer-grade neurofeedback products is based on the premise of self-responsibility.

Authors	Year	Participants	Interventions	Reported side effects
Hassan et al.[5]	2015	Seven spinal cord injury patients with paralysis and pain in the lower limbs.	Using a 16-channel electroencephalograph, audiovisual neurofeedback to promote relaxation and reduce lower extremity pain was administered 3-5 times per week, for a total of 40 sessions.	Three participants developed cramps in the lower extremities. Symptoms abated later that day.
Elbogen et al.[6]	2021	Forty-one veterans suffering from traumatic brain injury and PTSD.	Using a commercially available EEG headset and neurofeedback application, auditory neurofeedback to promote relaxation was administered four times per week for three months.	Discomfort due to headset (n=14), Drowsiness after training (n=13), Irritability (n=6), Headache (n=3), Dizziness (n=1), Tinnitus (n=1), Muscle cramps (n=14). All of the patients' symptoms disappeared when they stopped training.
Vuckovic et al.[7]	2019	Seven spinal cord injury patients with paralysis and pain in the limbs.	Using a commercially available EEG headset and feedback application, visual neurofeedback to promote relaxation for five minutes per session was given 5-6 times per day for two months.	Some participants felt headaches, plantar tingling, and hypersensitivity symptoms. Symptoms disappeared when training time was reduced.
Hershaw et al.[8]	2020	Thirty-eight veterans suffering from traumatic brain injury and PTSD.	Using a 19-channel electroencephalograph, a custom neurofeedback was administered 10-30 minutes per session, and was repeated for a minimum of 15 sessions within 6 weeks.	Two participants felt nausea and headache.

Table 2. Examples of side effects associated with neurofeedback intervention

Note 1) National Consumer Affair Center of Japan (NCAC) is an administrative agency that provides information and conducts research on consumer affairs from a comprehensive perspective, to create a stable and improved life for consumers, as well as contributing to their safety and wellbeing9. NCAC also undertakes Alternative Dispute Resolution (ADR) procedures to resolve important consumer disputes.

Note 2) In Japan, Relief Systems for Adverse Drug Reactions is a system that compensates for health hazards caused by adverse drug reactions that can occur even if the drug was properly used10. The purposes of the compensation include medical fees, disabilities, death, supporting the dependents of the affected person, and funeral expenses that were incurred due to the adverse drug reaction.

GQ3 What is neuromodulation?

Summary

Neuromodulation is the modification of neurological function, including both neuronal and glial cell activity, through delivery of a stimulus, such as electrical stimulation, magnetic stimulation, or chemical agents, to specific neurological targets[11]. Research and development in medical and research institutions is ongoing, and some technologies, such as deep brain stimulation and transcranial magnetic stimulation, are covered by public health insurance in Japan. On the other hand, neuromodulation products distributed for the general public are completely different from these medical/research-grade Neurotech products, and their methodologies, safety, and effectiveness have not been sufficiently established. A technology often found in consumer-grade products is the transcranial direct current stimulation (tDCS) device, which delivers weak direct currents via electrodes placed on the scalp. There are a lot of unknowns surrounding the potential risks of tDCS. Therefore, we recommend that the general public, without specialized knowledge, should not use consumer-grade neuromodulation products.

Explanation

What types of neuromodulation products for general consumers are available?

Neuromodulation products for general consumers mainly make claims for the following fields and uses[2] (Table 3). However, these claims are only made by the sellers on their websites or in their product catalogs, and their effectiveness has not been sufficiently verified.

Health Care

Relaxation / Sleep Improvement : Magnetic field stimulation promotes relaxation and sleep onset.

Appetite suppression : electrical stimulation of the mastoid process suppresses appetite through stimulation of the hypothalamus via the vestibular nerve.

Improved mood : electrical stimulation of the prefrontal cortex improves depressed mood.

Neuroprotective and restorative effects : transcranial and nasal irradiation of light at 10 Hz (near alpha-frequency band), protects nerves.

Capacity Improvement

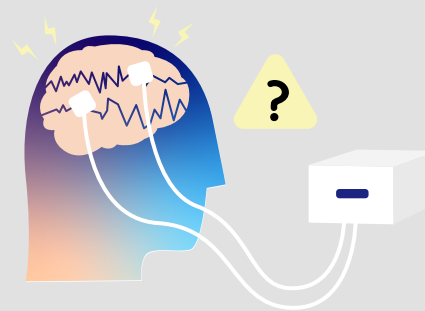
Improved motor performance : stimulates the motor cortex and increases the effectiveness of motor training for skill, speed, endurance, etc.

Improvement of cognitive function : Stimulation of the frontal lobe by generating micro-electrical signals with a headset temporarily improves cognitive function.

Caution: The above product examples are only one-sided claims made by the sellers on their websites or in their product catalogs. Whether the efficacy and safety of the products have been scientifically proven was not verified as a part of this guidebook. In addition, most of the products are sold overseas and have gone through a translation process into Japanese, but contain expressions that under the law and regulations, should be manufactured and sold as medical devices in Japan. Please thoroughly check the relevant laws and regulations when selling products.

An Example of Neuromodulation

Various physical stimuli are applied from outside the body to the central nervous system such as the brain, to adjust the function of the nervous system. Typical stimulation is through the use of electricity or magnetism. Recently, ultrasound and light stimulation methods have also been studied. Although the brain is the main stimulation site, there are also stimulation methods that aim to act indirectly on the brain by stimulating peripheral nerves such as the vestibular nerve. On the other hand, it is difficult for the general public to correctly set or adjust parameters such as the stimulation method, location, intensity, and frequency, which can be counterproductive or pose unforeseen risks.



Are neuromodulation products for general consumers safe?

The Guidebook Development Committee recommends that the general public, without specialized knowledge, do not use consumer-grade neuromodulation products. These products are different from those used for medical purposes; to add to the fact that their safety has not been adequately confirmed, because they work directly on the brain and nerves, both physically and chemically, they are considered to have higher potential risks compared to other Neurotechs. The efficacy of consumer-grade neuromodulation products also remains unclear. As an international expert opinion published in 2022 noted, companies manufacturing consumer-grade products are increasing sales of their products despite the effects of their products not being clear, because there are no strict screening processes for selling their products[12].

In Japan, as of 2022, neuromodulation products for general consumers have not been determined either applicable or non-applicable as medical devices, and there are no regulations or management systems in place for such products. Therefore, the user is responsible in the case that side effects or health hazards result from the use of neuromodulation. Considering that neuromodulation directly stimulates the brain and nervous system, and therefore poses the highest risk of health hazards among Neurotech products, we do not recommend its use until its efficacy and safety are confirmed. The Japanese Society of Clinical Neurophysiology has also cautioned, "The usage effectiveness of these devices has not been sufficiently verified scientifically[13]. As shown in the fact that there have been reports of cognitive decline with the use of commercially available tDCS devices, the safety of the devices themselves has not been sufficiently verified. No recommendations are made regarding the use of self-treatment devices and their protocols unless both efficacy and safety have been demonstrated by the International Federation of Clinical Neurophysiology." [14] Internationally, there are few reliable data on neuromodulation products for consumer use, and it is stated that further validation is needed[12]. Therefore, current neuromodulation technology should be viewed as a medical or research device to be used for specific purposes and with safety management practices, by medical and academic institutions. Casual use should be avoided.

GQ4

What should I be aware of with regards to commercial products?

Summary

Consumer Neurotech products can be purchased directly by the general public. However, it should be noted that unlike medical/research products, there is no system of approval or certification, and the frameworks for regulation or compensation of the products are not yet established, so use is at your own risk. There is a possibility that dangerous or dubious products with unknown efficacy may be on the market. When selecting a commercially available product, it is your responsibility to carefully evaluate whether the performance, effectiveness, and safety of the product have been thoroughly verified and explained, and whether a post-purchase support system is in place. Personal use of more dangerous neuromodulation products that stimulate the brain is not recommended.

Explanation

As of 2022, consumer Neurotech products sold for health promotion and entertainment purposes are sold through corporate e-commerce sites, major online shopping websites, and import agent shopping websites, and direct transactions by consumers are not regulated. However, unlike medical devices, their quality, efficacy, and safety are not verified by third parties such as the public sectors or specialized agencies. Since scientific support and certainty are not guaranteed, consumers themselves need to be more careful. Specifically, consumers should be aware of the following.

Confirm product safety and usage purposes

Since Neurotech is a product applied to the human body, safety is the most important aspect. Safety refers to both the safety of the product itself (e.g., "Is the device sharp enough not to injure the head?", "Is the output too strong and cause burns?", "Will it break easily?") and the safety of the effects on the human body when using the device (e.g., "Will it cause pain?", "Will it make me sick?", "Will it have an counterproductive effect?"). For product safety, it is desirable to confirm that products are designed, manufactured, and inspected for shipment in accordance with JIS (Japanese Industrial Standards), ISO (International Organization for Standardization), and IEC (International Electrotechnical Commission) standards for safe design of industrial products. However, since this is a voluntary standard, not following the standard does not immediately mean that the product is unsafe. Since the effects on the human body vary depending on the technology, please refer to GQ2 "What is Neurofeedback?" and GQ3: "What is neuromodulation?" for more information. Next, carefully read the product's functions and intended use to see if it affects the structure and function of the brain and nerves. For example, a Neurotech product such as "a program that detects physiological information such as brain waves to control air conditioners, alarm clocks, and music players" would pose little danger because it is not trying to affect the body or brain in any way. However, we cannot rule out the possibility that even these products may cause side effects such as headaches or brain fatigue beyond what was initially anticipated, due to trying to use the brain as hard as possible. If any unusual symptoms occur, stop using the product immediately and seek medical attention. Afterwards, please report to the National Consumer Center that you have experienced a change in your health condition.

On the other hand, if a consumer Neurotech product appears to be making claims on affecting the size, shape, or function of the brain, such as "preventing brain atrophy" or "improving cognitive function," use with caution. This is because such products must undergo a rigorous review process as a medical device before it can be sold (Appendix 1). If the product has not been approved or certified as a medical device, the scientific evidence for its effectiveness in changing brain structure and function is insufficient. In the first place, since there is no mechanism or institution to test for efficacy and safety, it is up to the company to decide whether or not to conduct sufficient verification, and it is up to the users themselves to determine them.

GQ4 What should I be aware of with regards to commercial products?

Correctly understand the meaning of the written "effect"

It is also important not to have an exaggerated interpretation of product effects and not to have an overly high expectation. For example, if a product claims that it is "expected to improve concentration," this only means that "it was created with the expectation of such an effect, but it has not yet been proven that it really does so". If a published paper or in-house research has verified the effectiveness of the product, it would be beneficial to correctly understand under what conditions, with whom, and in what way was the product used, for an improvement in which functions, and to what degree. Even if an improvement in concentration has been observed in one limited situation, it is not for certain that the same effect will be seen in other situations, such as in studying or sports. Also, if individual characteristics such as gender, age, and their original cognitive or motor abilities are different, it is uncertain that the same effect can be expected for everyone. It is necessary to read the product description carefully and correctly understand what is known about the product.

Based on these considerations, we believe that the following conditions are essential for a reliable Neurotech product (Box 1). We recommend that you thoroughly check these points when selecting a Neurotech product.

Three checkpoints to select a reliable Neurotech product

☑ ① Product reliability
→ Has the efficacy, safety, and performance been verified using the product? If a product is not properly tested for effectiveness, it may not be effective even when used correctly.

☑ ② Reliability of the technology
→ Is information about risks and how to address risks provided? Please check if the user manual describes anything regarding usage that should be followed, such as the recommended time of use per day. Besides, information on the scientific basis and limitations should be disclosed in an appropriate and detailed manner.

☑ ③ Reliability of the seller
→ Is a support system in place? Post-purchase follow-up, such as a contact person, would be a great help for general consumers if something goes wrong. In other words, the seller should have a post-purchase follow-up system in place, including having a contact point for inquiries and conducting recalls if necessary.

GQ4 What should I be aware of with regards to commercial products?

Reliability of the product itself - First, let's check the performance, effectiveness, and safety of the device itself

• Is the accuracy of the measurement equipment and signal processing acceptable?

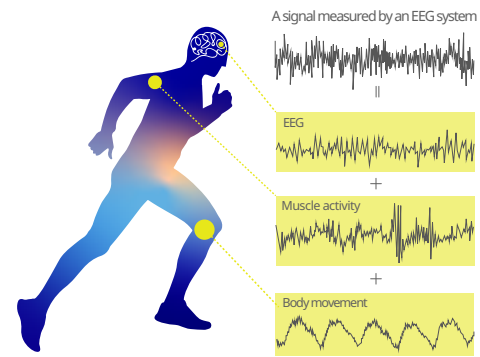
Here, we will discuss the reliability of signal quality, that is, whether the equipment is able to accurately record brain activity (biological signals), and the reliability of signal processing, that is, whether the signals obtained inside the machine are correctly processed. EEG, the most commonly used method of recording brain activity, is a weak biological signal that is easily mixed with noise, making it difficult to record accurately. Therefore, there are many considerations that must be made in order to correctly record EEG signals.
First, the EEG electrodes are checked for proper placement on the head. In addition, the electrodes must be designed for the purpose of EEG measurement and must have a mechanism to hold the electrodes securely in place. Consumers are required to maintain the correct posture during the measurement and to be aware of noise sources in their surrounding environments (e.g., conduction/ radiation noise and physical vibrations). Even when correct signals are obtained, the signal processing, such as noise reduction and the creation of brain decoding models, must be accurate. As described, the correct brain state may not be estimated due to various factors such as the device itself, signal processing, consumer usage, and the environment in which the device was used. A product that displays the actual measured EEG and allows the user to check and make adjustments on whether it is being measured and processed correctly would be more reliable.
Although the reliability of such measuring instruments and information processing is often not known from the outside because they are not required to be labeled, it is meaningful to evaluate reliability from the perspectives described above. This is an area where manufacturers should make efforts to disclose information with more transparency.

• Has the product itself been used to verify its effectiveness through scientifically sound procedures?

When selecting a Neurotech product, whether or not the product itself has been used to verify its effectiveness is another important piece of information to determine its credibility. For example, for a product to claim to improve muscle strength, it must be shown through scientific validation that "muscle strength actually improved significantly when the product has been used" . In addition, it is preferable for the process and results to be reviewed (peer-reviewed) by a third party, approved, and published as an academic paper. As mentioned above, a good rule of thumb is whether the verification of the product's effectiveness has been published as a peer-reviewed academic paper. However, since the quality of papers varies, the existence of a paper does not necessarily provide sufficient evidence. Therefore, in the future, it would be beneficial to have a third-party committee that can further verify the validity of the product.
A 2019 international study examined 41 different consumer Neurotech products and found that only 8 had scientifically verified the product's claimed benefits and published them in a paper[15]. Additionally, 29 of the products made it appear as if they had evidence by having links to websites or articles that provided scientific evidence[15]. However, the articles were about the results of using similar products, and no verification was conducted using the product itself. Of course, it is possible that those products are also effective, but there is insufficient certainty. Confirming whether the effectiveness of a product has been verified using the product itself is very important in order to determine the reliability of the product.
In fact, making excessive claims can violate Article 5 of the Act against Unjustifiable Premiums and Misleading Representations (see Note 3), which prohibits misrepresentation, misrepresentation of quality, and misrepresentation of advantage, as is the case with health foods and health appliances, and can be the subject of disciplinary action. However, there are also some labeling that cleverly manipulates impressions, and consumers themselves need to be more careful in judging the effectiveness and safety of such labeling.

EEG is prone to noise

EEG is a difficult biological signal to measure because it is easily mixed with noise (i.e., components other than EEG). For example, when a person walks or moves, noise from muscle activity and physical vibration are contaminated into the EEG signal. If these are not removed from the "EEG" data, it may lead to incorrect results. A product that carefully explains how to correctly measure brain waves and allows the user to check the actual signals will be more likely to produce the correct effect.



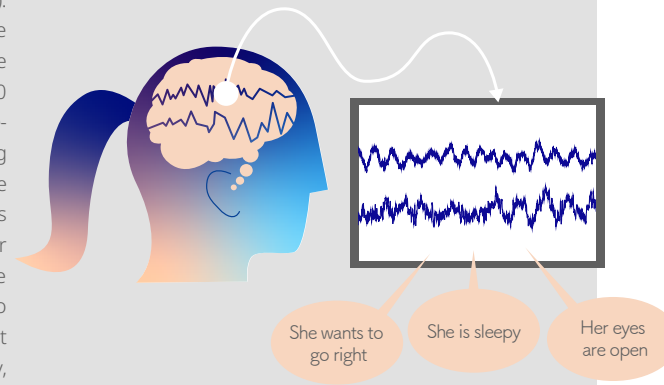
What should I be aware of with regards to commercial products?

Reliability of the technology itself - Is it even possible with current neuroscience?

The sales websites of Neurotech products claim a wide variety of functions. However, are they really feasible with the current understanding of neuroscience? The validity of these functions must be carefully verified. It is a common understanding among researchers that although an increasing amount of things can be accomplished using neuroscience, there are still many things that we do not know about or can only partially achieve. We don't know if the features claimed by Neurotech products are scientifically valid. In other words, it is necessary to evaluate how reliable the neuroscientific evidence and technology used by these products, currently are. For example, with current technology, it is not easy to accurately read sophisticated thoughts, personalities, and complex emotions from brain waves. Specifically what and how much can be done will be covered in the Evidence Book to be published soon. We recommend that you evaluate how reliable the neuroscientific evidence and techniques used in the products currently are, referring to the Evidence Book. Online information can also be helpful if they are reliable sources of information (Appendix 3). Note that products that do not even describe what kind of neuroscience technology they use (so-called black box products) are less reliable because it is difficult to evaluate and judge them from the outside. For all Neurotech, scientific transparency is an essential element.

What can we read from the EEG?

This picture shows a person measuring their brain activity (EEG). EEG is recorded as a continuous wave "signal" as shown in the figure. It does not measure the activity of individual neurons (the brain' s nerve cells), but only the synchronous activity of 10 to 100 million cells, and the activity of many cells is averaged out. Therefore, it only reads out fragmentary information; the EEG recording systems with a small number of channels, such as those that are commercially available, can only decipher general brain states such as "are the eyes open or closed", and "is the user sleepy or awake", and general movement intents such as "whether the user wants to go right or left", or "whether the user is trying to move a device, appliance, or game". Current technology has not yet reached the point of analyzing the full range of brain activity, and scientists believe that this is likely impossible with today's technology.



Note 3) Act against Unjustifiable Premiums and Misleading Representations (Act No. 134 of 1962), as defined under Japanese law, was created in order to protect the interests of general consumers by preventing their inducement by means of unjustifiable premiums and misleading representations with regards to the transaction of goods and services, this Act places limitations on and prohibits acts that are likely to interfere with general consumers' voluntary and rational choice-making.

What should I be aware of with regards to commercial products?

Reliability of the seller-
Does the seller provide a comprehensive explanation of the product and support system?

When selecting a distributor of Neurotech products, an important aspect to consider is whether the company is honest in its disclosure of information to you, the consumer. Specifically, does the website or instruction manual provide a thorough explanation of how the product is used, how its functions are verified, and the risks involved? For example, the company must have a support system in place with clear and sufficient information disclosure, such as product description, scientific basis, usage, risks of use, related knowledge, contents of ethics committee review, glossary, customer feedback, frequently asked questions, and customer support contact.

Suppose the product itself is defective (i.e., lacks the safety that a product should normally have) and causes damage to life or health. In that case, the Product Liability Law (PL Law) may be used to seek compensation from the manufacturer, or for imported products, from the importer. However, the consumer must prove a causal relationship between the defect and the health hazard, and even if the claim is approved, there is a possibility that overseas manufacturers or small start-ups may not be able to immediately provide adequate compensation.

Furthermore, side effects may occur even if the product is not defective and is used according to the instruction manual. While there are public compensation programs such as the Japanese Postmarketing Relief Systems for Adverse Drug Reactions (see Note 2), for side effects that occur despite the correct use of a product approved as a drug, public compensation for health hazards is not applicable to consumer Neurotech products because they are not approved as a medical device.

Compensation and support systems are common issues to all non-medical devices in general, but compared to health devices such as those used for resistance training and relaxation devices, Neurotech products require even greater caution because the risks are not yet well understood (Appendix 2). For this reason, consumers must use them at their own risk, referring to alerts issued by academic societies, notifications from the National Consumer Center, or online sources about related issues. When selecting a product, it is important to carefully read the descriptions about the post-purchase support system and choose reliable distributors and products.

GQ5 What should I keep in mind when developing a product?

Summary

This section is intended not for the general public, but for companies that are considering operating a business using Neurotech products or services. As we have shown in this document, several issues have been raised internationally regarding Neurotech products for general consumers, such as assuring their quality, safety and efficacy, management and protection of privacy, and establishing follow-up systems[15]. The ethical and moral responsibility to assure these is required of businesses and industry associations. Even without waiting for legislation, it would be desirable for industry associations to voluntarily establish standards and build a system to enforce compliance. More responsible information disclosure and communication with consumers will be essential for Neurotech to become a technology trusted by society.

Explanation

Challenges identified internationally for Neurotech businesses

Issue 1. Insufficient verification and information disclosure on efficacy and safety, which may lead to misunderstanding by general consumers.

General consumers are not able to verify the validity of the effects claimed by Neurotech products on their own. It is desirable for businesses as providers to verify the effectiveness, performance, and safety of their products, disclose the results in detail, and establish a sales system that enables consumers to correctly judge the effectiveness and safety of their products[16]. Even if validation tests have been conducted, it may be uncertain whether results obtained in a controlled experimental environment are directly applicable to consumer-grade products used in everyday life. In addition, it is essential to have appropriate control groups, experimental settings, and experimental designs in order to demonstrate the effects of a product. For example, to show that a product reduces pain, it is necessary to prepare sham products that are indistinguishable from the real product to the user, test both real and sham products under the same conditions, and show that the real product reduces pain better than the sham product. This is to show the product is more effective than the placebo effect of experiencing pain suppression simply by using a sham product. So, what points should we be aware of in validations in order to say that we can trust the claimed effects of a product or service? Scientists generally verify reliability by checking the following points (Box 2).

- The design of the experiment: What kind of design was used? Are biases and confounds controlled?
- Who is being tested: Effects may be different for different ethnic groups, ages, genders, and personality traits.
- Subject recruitment methods: Are recruitment methods appropriate? Free from conflicts of interest (COI) or any other potential biases?
- Individual differences: There may be individual differences due to genetic diversity or differences in brain characteristics.
- State of participant: Effects can vary due to the participants' mental state, physical conditions, diurnal variation, hormonal status, etc.
- State of verification performed: Under what circumstances, how much, and how often?
- Pre-registration: Has the research hypothesis and data collection/analysis plan been submitted to a third party before collecting data?
- Monitoring: Is a third-party oversight system in place for the verification process?
- Data publication: Is the actual verification data itself available to the public?
- COI disclosures: Are COI disclosures being made appropriately?
- Comparison with other methods: Between traditionally available methods and the new Neurotech product being tested, which one would be recommended, based on a comprehensive comparison of factors such as whether other traditional methods would achieve the same effect, and the hurdles in the implementation of new technology?
- Generalizability of the results: Can the results that were directly verified be expected to have the same effect under other conditions?

Issue 2: Ambiguous definitions of effectiveness or making claims beyond the limits of neuroscience.

Abstract terms such as concentration and stress are received in different ways by consumers. For example, when someone says "improved concentration," some may think of improved focus while working, while others may think of improved performance in sports, improvement from distraction due to disability, and many other effects. It is thought that instead of only mentioning the improvement in concentration, also providing an explanation of specifically what it is effective for, and in what circumstances, would prevent excessive expectations and misunderstandings. It is also important to explain how effective they are, including the effect size. If it only stated, "it was effective," consumers may expect a near 100%, immediate improvement. Since there is a considerably wide range of effects, it is necessary to mention what specific effects were confirmed, such as whether the effects are noticeable, whether they produce behavioral changes, what percentage of people benefited, how strong the effects are compared to other standard methods, and whether the effectiveness of the method changes when used in combination with other methods.

Issue 3: Lack of communication about possible risks and countermeasures.

Even within "Neurotech," different risks can be associated with different technologies and products, and there are many things we do not yet know. For example, in the case of electrical stimulators, there may be physical harm such as burns, and in the case of products that use EEG, there may be psychological harm where inaccurate measurements provide untrue results and consumers are driven by unnecessary anxiety (such as becoming anxious when they are labeled as stressed when they are not really stressed). It has been pointed out that half of the products on the market overseas do not adequately describe the involved risks and what to do if the condition worsens[14]. Please see Appendix 2 for more information. Businesses are expected to be willing to communicate with consumers by fully explaining possible risks and providing a post-purchase support system.

Issue 4: Issues related to privacy and identity in using brain information.

Brain signals obtained by measuring brain activity can be considered personal information if they are managed in combination with information that can identify the subject. On the other hand, it is difficult to identify the subject based on the brain signals alone, and at this stage, they are not considered personal information and are not regulated. However, sales, resales, or third party usages of these data without the consent of the subject is undesirable. Furthermore, there are recent reports that individuals can be identified with a certain degree of accuracy from EEG characteristics[17,18], and depending on future technological developments, it may become necessary to strictly treat brain signals as personally identifiable information, even on its own. In addition to the issue of privacy, it is necessary to take measures to prevent prejudice and discrimination if it becomes possible to determine a person's personal preferences and abilities from neural data.

What should I keep in mind when developing a product?

Measures to consider when running a Neurotech business

In order to address the issues noted above, the Guidebook Development Committee suggests, as an example, that sellers consider the following items. Please note, however, that these items are not a complete list of necessary requirements.

1. Check the relevant laws and regulations and confirm whether or not the device is considered as a medical device

As described in Appendix 1, in Japan, Neurotech products (both hardware and software) may be categorized as medical devices depending on their mechanism or purpose. Although defined in writing, Regulations under the Pharmaceutical and Medical Device Act do not draw a clear line in operation, and applicability tends to be judged comprehensively based on the mechanism and function of individual products, the intended use, and reports of health hazards. Especially in the developing Neurotech market, it is undeniable that a product may become subject to regulations after its launch, depending on the accumulation of future findings and damage reports. When developing and marketing a product, it is recommended to thoroughly check the relevant laws and regulations, and if necessary, consult with the Pharmaceuticals and Medical Devices Agency (PMDA, see Note 4), the Pharmaceuticals Division of each prefecture, or officials in the pharmaceuticals division of other local governments.

2. Ensure safety as a manufactured product and biological safety

Since Neurotech products are industrial products that are applied to the human body, it is necessary to ensure the product is defect-free (safety as a manufactured product) and that no adverse effects on the human body when the product is used (biological safety). For safety as a product, it is desirable to comply with industrial standards such as JIS (Japanese Industrial Standards), ISO (International Organization for Standardization), and IEC (International Electrotechnical Commission). If there is no appropriate standard, it is desirable to start by establishing a new standard.

With regards to biological safety, carefully investigate and disclose whether any side effects or adverse events have ever occurred in similar products or technologies. In addition, under the review and advice of the Ethics Committee, verify the efficacy and safety of the product by conducting Proof-of-Concept studies using the product in question in an ethically sound manner. In particular, if there is concern about the effects of the product on the human body, it is desirable to establish a research system that includes physicians.

3. Disclose the performance of the hardware device

1) Basic device performance specifications: material and number of electrodes, electrode position, sampling frequency, dynamic range, bit rate, etc.
2) Accuracy of measurement and discrimination: signal-to-noise ratio or quantitative index which reflects signal quality (e.g., accuracy of discrimination between open/closed eye states from oscillatory signal or between Target/Non-Target from ERP P300 amplitude.)

4. Disclose the validation method of effectiveness and its expected value

There are several methods to validate effectiveness. The methods are listed in order of recommendation.

A. A study is conducted for the purpose of validation, and the results are peer-reviewed by third-party experts before being published as an academic paper. Note that research for the purpose of validation is usually considered to be more correct when the results of multiple studies are gathered.

B. Even without publishing it as an academic paper, conduct tests for the purpose of validation, publish the results as they are, and publish objective evaluations by third parties such as experts.

C. If the test itself for verification is difficult, cite relevant academic articles from literature to carefully explain the validity and risks. In this case, however, it is desirable to publish it alongside an accompanying statement of experts' evaluation of the following points.

-The product itself was not used for the verification, so there is no guarantee that it will have the same effect as the cited sources.

-Under different usage conditions and equipment, what are some possible differences in the effectiveness of the product? (e.g., an explanation on the possibility of unforeseen risks)

In addition, it is recommended that the following information be clearly stated when disclosing verification results.

-Existence of evidence of the claimed effects and media in which results were published.

-Participants' information: how to determine the number of samples, the method of recruitment, and the attributes of participants.

-Design of the study: as detailed a protocol as possible, especially information about the control group condition.

-Experimenter: whether a third party is involved, whether the experimenter is skilled, etc.

-Methods of data processing: specific statistical method, etc.
-Evaluation items and indicators employed to verify claims: whether they are subjective indicators, behavioral indicators, or other biomarkers.
-Exact effects of using the product: difference from control condition, effect size.

5. Define the expected effects in detail and describe them correctly to avoid misunderstandings or excessive expectations

As mentioned above, general and abstract claims can lead to misunderstandings and excessive expectations since the interpretation of such claims is left to the consumer. Therefore, it is recommended to use easy-to-understand expressions and describe in detail what is confirmed by what kind of validation, what can be changed, how, and to what extent. It is also desirable to carefully describe what has not been verified, what could not be done, or what could not be understood (e.g., it has not been tried on young people or in different environments, there are large individual differences because half of the people did not find it effective).

6. Include warnings in the instructions to avoid unintended use or misuse

Since Neurotech is a new technology that has not yet permeated our daily lives, it is necessary to carefully explain how to use it correctly, and furthermore, to take measures to prevent unintended use or misuse of the technology. It is recommended to provide tutorials with videos, documents or other references to ensure correct use. Preset monitoring programs that can mechanically check if the device is actually being used correctly, are also recommended.

7. Describe possible risks and ways to handle them, and provide a contact address for inquiries

There are risks associated with the use of Neurotech, as described in Appendix 2. Since risks themselves exist with any technology, it is important to explain to consumers in advance the possibility of such risks and ways to deal with them, and to establish a system that allows consumers to decide whether or not to use the product after fully understanding and agreeing to the risks. It is also recommended that a contact or inquiry form be established to provide a system for answering any problems or concerns that may arise after purchase.

8. Publish compliance guidelines for privacy and rights protection

It is recommended that you establish and post privacy and rights protection policies, and this applies not only for Neurotech, but for all modern technologies including AI-based products. The following are particularly important for Neurotech.
-Handling and protection of information regarding an individual' s brain and information obtained through use of Neurotech.
-Security assurance to protect against unauthorized use without consent.
-Facilitating opportunities for individuals to choose how their data is used and will be retained, including options for access, correction and deletion of personal data.

9. When conducting research and development, cooperate with medical and research institutions and other research organizations, and comply with ethical standards

When conducting research and development, it is desirable to proceed in the form of joint research with research institutions, and to verify efficacy and safety in an ethical manner under the review and advice of an ethics committee. In particular, if there is concern about effects on the human body, it is desirable to establish a research system that includes physicians. The ethical and moral obligation to reduce the uncertainties and resolve the challenges associated with Neurotech, as discussed in this document, lies with the developer, not the consumer. While cost and effort may be a concern, please consider careful development of Neurotech so that it becomes a trusted industry.

Note 4) Pharmaceuticals and Medical Devices Agency (PMDA) is a Japanese regulatory agency with the aim of protecting public health through assuring the safety, efficacy, and quality of pharmaceutical and medical devices10. Its main functions are providing relief compensations for health hazards, approving pharmaceuticals and medical devices for marketing authorization through conducting scientific reviews, and monitoring their post-market safety.

Appendix 1 Definition of medical devices and treatment of consumer Neurotech products

Remark: This Appendix contains topics related to pharmaceutical laws and regulations in Japan. The following contents may only apply in Japan.

Are consumer-grade products not considered as medical devices?

Article 2, paragraph 4 of the Pharmaceutical and Medical Device Act (see Note 5) refers to medical devices as, "appliances or instruments, etc. which are intended for use in the diagnosis, treatment or prevention of disease in humans or animals, or intended to affect the structure or functioning of the bodies of humans or animals (excluding regenerative medicine products), and which are specified by Cabinet Order[19]." In other words, Neurotech products that are intended to diagnose, treat, or prevent diseases or to affect the structure or function of the body, that are also specified by a Cabinet Order (Article 1 of the Order for Enforcement of the Pharmaceutical and Medical Device Act; Cabinet Order No. 11 of 1961), are classified as medical devices. Medical devices must be approved and certified by the law with respect to the quality of the product itself, the effectiveness of the device' s impact on humans in diagnosis, treatment, and prevention of medical conditions, and the safety and usage method of the device when used on humans. Only medical device manufacturers and distributors are allowed to manufacture, import, and sell medical devices in the domestic market, and only devices that have been verified for quality, efficacy, and safety and approved, certified, and notified by the Minister of Health, Labour and Welfare or a third-party certification body are allowed to be sold. If the product is considered as a medical device, it will be marked as such. It will be labeled with either its approval number, license number, certification number, or notification number.

Does that mean a Neurotech product that uses brain waves to control a game does not need to be approved as a medical device? If one only superficially reads the text of the Pharmaceutical and Medical Device Act, which states, "appliances or instruments, etc. intended to affect the structure or function of the human or animal body," any device intended to affect human function can be considered as a medical device. From this definition, a product that merely operates a game using brain waves would not be considered as a medical device. However, since the purpose of the Pharmaceutical and Medical Device Act is to protect the public from health hazards, the law, cabinet orders, and their interpretations are flexibly revised as needed. There are no clear standards or lines regarding the applicability of medical devices, so decisions are made based on a comprehensive review of factors, including product characteristics, reports of damage, the accumulation of new knowledge, and technological advances. Neurotech products for general consumers that are currently not considered as medical devices by the national or prefectural governments will be subject to the Pharmaceutical and Medical Device Act if any effects on brain function or side effects are revealed in the future.

Applicability as a medical device is not clear-cut, and is determined comprehensively

Appendix 1

Definition of medical devices and treatment of consumer Neurotech products

What should I be aware of when a product is not a medical device or its applicability is unknown ?

For Neurotech products that are not labeled as medical devices or are unclear, it is advisable for the general public to first confirm whether they are indeed not applicable as medical devices. This is because some Neurotech products that claim not to be medical devices may affect the structure and functions of the human body, and if used incorrectly, it may cause health hazards. Products that are marketed and claim indications and effects similar to those of medical devices without approval are considered as unapproved medical devices and may be subject to apprehension.

Here we introduce what to do if you see a suspicious product suspected of being an unapproved medical device or if you experience a health hazard. To be approved as a medical device, a product must undergo a review by the Pharmaceuticals and Medical Devices Agency (PMDA)[10], an independent administrative agency that is responsible for performing the three functions of health hazard remedy, approval review, and creating safety measures, with regards to pharmaceuticals and other products. On the other hand, the Compliance and Narcotics Division of the Ministry of Health, Labour and Welfare's Pharmaceuticals Safety and Environmental Health Bureau and the Pharmaceuticals Divisions of prefectural governments (click here for a list[20]) are in charge of regulating pharmaceutical affairs for products that are already on the market. The "Ayashii Yakubutsu Contact Net" [21] provides consumers with information and a contact point for reporting incidents. If you find a Neurotech product for general consumers that is an unapproved medical device intended to diagnose, treat, or prevent a disease or affect the structure or function of the body, such as "brain stimulation," please report it to these helplines. Let us make society a place where safe and secure Neurotech is nurtured through smooth cooperation between industry, government, academia, and the private sector.

If you experience any health hazards, please seek medical attention immediately. At the same time, please keep a detailed record of which product was used, as well as when, what kind, and to what extent symptoms occurred, along with other information such as photographs. Report the information to the above helplines or the National Consumer Center.

【Contact points for reporting suspected medical device products】

①If the address of the business is known from its website, or other such sources
If you know the prefecture, the city or special ward where the business has its address, please contact the respective local government. Contact e-mail addresses and other information can be found in the Ministry of Health, Labour and Welfare's "Request for Information on Internet Sites Suspected of Violating the Pharmaceuticals and Medical Devices Act" .

②Cases where the address of the business is unknown or is an overseas business
Please contact one of the following.
a. Contact the "Ayashii Yakubutsu Contact Net" by phone or report form.
Contact: +81-3-5542-1865 or https://www.yakubutsu.mhlw.go.jp/#form
b. Contact the Compliance and Narcotics Division of the Ministry of Health, Labour and Welfare's Pharmaceuticals Safety and Environmental Health Bureau by email.
yakuji-net@mhlw.go.jp

【Information on unapproved and unlicensed drugs and health hazards can be found at:】

①Ministry of Health, Labour and Welfare website, "Information on Unapproved and Unlicensed Drugs." (https://www.mhlw.go.jp/stf/kinkyu/diet/musyounin.html)
②National Consumer Center Website.
(https://www.kokusen.go.jp/)

Note 5) Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices (Act No. 145 of 1960), also called the Pharmaceutical and Medical Device Act, was added to the Japanese law with the purpose of improving public health and hygiene. This law allows for conducting the necessary regulations to ensure the quality, efficacy and safety of pharmaceuticals, quasi-pharmaceutical products, cosmetics, medical devices, and regenerative medicine products, and for preventing the occurrence or spread of health-related hazards due to usage of these products. It also includes taking measures against designated substances, and taking necessary measures for the promotion of research and development of pharmaceuticals, medical devices and regenerative medicine products that fulfill high medical needs.

Appendix 2

Risks and ethical issues associated with the use of Neurotech

Summary

Risks are different depending on the type of Neurotech product. BMI and neurofeedback products, which measure brain waves and other signals and output them to a machine, are considered to have a low risk of serious side effects if used properly. On the other hand, neuromodulation-type products that apply stimulation to the brain are considered to have relatively high risks to the body, and it is recommended that laypeople refrain from using them. Furthermore, since Neurotech targets the brain, a special organ that controls the human mind (personality and identity), there are unique risks and ethical, social, and legal issues that are not present in other technologies. Because it is a developing technology, new risks may emerge as the technology progresses. It is necessary to use Neurotech with caution while gathering information and recognizing that there are still unknown and unresolved issues.

When using these products, keep and follow the established methods and ranges. Even if the change seems meaningless at first glance, the effects on living organisms may change drastically in unexpected ways, so great care must be taken.

Explanation

In the Ethical Guide to BMI Research[22] published by Japanese researchers, it is thought to be essential to consider the following risks when using Neurotech:

1) Risks associated with technology and devices intervening in brain function.
2) Time, physical, and mental strain that occurs while becoming familiar with novel technology and devices.
3) Psychological burden and anxiety may arise due to the user's inability to use the technology and devices properly.
4) Daily life can be transformed with the use of technology and devices.
5) Current science cannot always predict the effects of long-term use of novel technology and devices.
6) Measures are not fully in place to ensure the safety of the technology and devices and to reduce the above burdens.

In addition to these issues, because the brain is a special organ that controls the personality and mind, unique ethical, social, and legal issues that do not exist with other technologies can arise. While international discussions are underway to resolve these issues, many have yet to be resolved as of 2022. As technology develops, the industry, government, academia, and the private sector must engage in discussions to establish rules and shared understanding. In the following, we will discuss the particularly important issues of risks associated with intervening in brain functions and ethical issues. For more information on other topics, please see the Ethics Guide for BMI Research[22].

Risks and ethical issues associate with the use of Neurotech

What are the risks of intervening in brain function?

When considering the risks associated with Neurotech, it is necessary to distinguish between risks to the body, such as pain and itching, and risks to brain function. The risks to the body vary depending on the type of technology and can be referred under GQ2 "What is Neurofeedback?" and GQ3 "What is Neuromodulation?" Typical risks to brain function include the following.

1. Unexpected changes may be irreversible

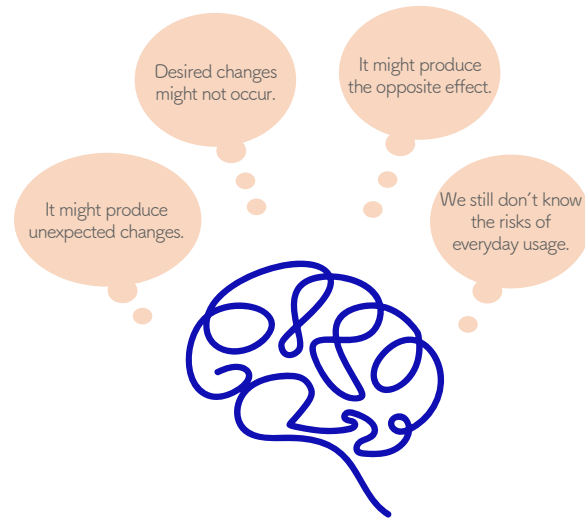
Neuroplasticity refers to the brain' s ability to change and maintain the change. In other words, if the brain is changed through training or other means, it is not known whether the original (pre-training) state can be restored, even if undesirable side effects occur. In addition, once the brain is altered, it may not return to its original state (irreversibility). There is no known way to immediately reverse the changes when the results are unexpected. This point needs careful consideration. Of course, if good changes occur and are maintained, it may be possible to resolve issues that previous methods could not resolve. However, it is important to note that irreversibility can work for the better or for the worse.

2. It may not produce the expected effects or may even produce opposite effects

Even for the technology and devices that have been scientifically proven to be effective, unforeseen factors (e.g., weather, the person's physical characteristics, and physical condition) may prevent the reproduction of the same results. This is called the reproducibility problem. For example, even if the same methods were used as described in the paper, the same results may not be obtained due to some factors. This has also been a problem in studies using medical devices on human subjects. In worse cases, the opposite effect of the intended outcome (e.g., loss of concentration, an increase in stress) may be produced. However, it is unknown why these phenomena occur and under what conditions they can be prevented. It is important to know that the brain responds more unpredictably than any other organ, and experienced effects differ between individuals.

3. The risks associated with daily and long-term use are yet unknown

The risks identified to date have occurred in studies that have been carefully conducted under the supervision of medical or research institutions, with the approval of ethics committees. When we use the products in our daily lives, previously unreported risks may occur. In particular, the potential risks associated with long-term use of the product have not been studied on a larger scale, and reviews regarding safety need to be more comprehensive. As technology progresses, new products may be developed, and new risks may arise. When using a product, careful use is recommended by closely monitoring daily changes and consulting an inquiry desk or healthcare providers if any abnormalities occur.



Risks and ethical issues associate with the use of Neurotech

What ethical issues are involved?

Ethical challenges can be brought with any technological development. Many ethical issues raised in neuroscience research are in common with those in other fields of science and are not unique[23]. However, Neurotech deals with the brain, a specialized organ that controls the personality and mind. Therefore, there are unique challenges, such as the protection of privacy, including thoughts and feelings, threats to personal will, and violations of self-determination. These issues are the subject of much international discussion (see Note 6) but have yet to be resolved. These challenges must be recognized not only by Neurotech developers but also by the consumers who want to use them. In order to solve these issues, it is important to aim for consensus building through discussions and collaboration between the industry, government, academia, and the private sector, in parallel with technological development. This section introduces ethical issues that should be considered when using consumer Neurotech products.

• Concerns about enhancement (artificially improving abilities)

When Neurotech products are used in daily life for the purpose of enhancing human abilities themselves, there are concerns, for example, about whether it is morally permissible to enhance abilities that were originally impossible for humans, whether it would be a form of doping in sports, and whether it would be an impermissible intervention to the human body. Concerns also lie in the possibility of inequality between those who do and do not engage in enhancement, as well as the widening gap between the rich and the poor due to their differences in abilities to access technology.

On the other hand, the effects and scope of what can be achieved with currently available commercial Neurotech products are not large. For more information, please refer to the forthcoming Evidence Book and the review[12] on neuroenhancement by brain stimulation experts. The actual effects on the body are estimated to be comparable to those of other enhancement techniques (e.g., strength training, electrical stimulation of skin and muscles, coffee, and taking dietary supplements) and are not as powerful and immediate as doping with drugs. Neurotech is often associated with doping, but as of 2022, no Neurotech products are listed on the World Anti-Doping Code. However, the situation may change with advances in technology, so it is advisable to check for the latest information.

Note 6) For example, in parallel with the development of advanced neuroscience technologies, the BRAIN Initiative (Brain Research through Advancing Innovative Neurotechnologies Initiative) promoted in the U.S., is developing guidelines to address ethical issues that were brought up by the U.S. Presidential Commission for the Study of Bioethical Issues.

Risks and ethical issues associate with the use of Neurotech

• Privacy concerns

Brain signals obtained by measuring brain activity may contain sensitive information because they are information from the brain which controls thoughts and personality. Thus, there may be concerns about privacy, such as "Thoughts and feelings may be read" and "Thoughts may be misused." In fact, it is possible, though not 100% accurate, to determine general brain states such as "Are eyes open or closed?" or "Sleepy or awake?" and general motor intentions such as "Do you want to go right or left?," or "Which device, appliance, or game are you trying to move?" On the other hand, it is not yet possible to estimate advanced thoughts, personalities, and complex emotions, such as, "What are they thinking right now?" or "What are their personalities, interests, and hobbies?" It is impossible to read everything from brain signals and we are only able to estimate vague physical or mental states by mathematically processing extremely weak signals. Therefore, there is no need to be overly concerned about privacy when using Neurotech products for general consumers at this time. However, as Neurotech becomes more widely used, more functions will likely be achieved, and discussions should be held in parallel with development.

There is also progress in the development of technology that aims at identifying individuals using their brain signals. Some have suggested that brain signals alone, without any other identifying information, should be treated as personal information. Although personal identification is considered difficult to achieve with the current technology due to its low accuracy, it may be achieved in the future.

Although ethical issues related to Neurotech, such as the ones mentioned above, are being debated around the world, no unified guidelines or viewpoint has been reached. Since the responsibility for proactively resolving ethical issues lies not with consumers but with the industry, it is imperative that they take the initiative to recognize these issues, take action to address them, and apply measures to protect consumer rights and privacy. Particularly, when conducting research and development, it is recommended to proceed in collaboration with medical or research institutions and to proceed with ethical standards under the review and advice of an ethics committee. On the other hand, having consent based on the proactive understanding on the consumer side is also essential. It is necessary to aim for the sound development of the industry through repeated discussions and consensus building among industry, government, academia, and the private sector, and establishing rules in a manner similar to setting voluntary self-imposed standards (see Note 7) without waiting for legislation.

Note 7) An example from another field is the "Voluntary Standards to be Observed by Businesses Handling Personal Genetic Information" . The Association of Genetic Information (https://aogi.jp/), which developed the standards, was established to enable consumers to select technically, ethically, legally, and socially respectable and appropriate genetic testing services, to promote the provision of easy-to-understand and appropriate genetic testing services by businesses to consumers, and to ensure that genetic testing services are properly understood and permeated soundly through society. As described in the above example, it is expected that companies and other entities that sell products will voluntarily establish rules to promote the sound development of the industry.

Appendix 3

How to get the latest information on Neurotech

Summary

There are three primary sources of information about Neurotech. The first is the latest news from companies and media outlets. Mass media, marketing companies, and more recently, individual researchers and experts are broadcasting news about neuroscience. The second is the latest academic papers published in peer-reviewed neuroscience journals. The third is statements and other documents issued by public organizations such as the Organization for Economic Co-operation and Development (OECD). Some publishers and organizations send out up-to-date e-newsletters or provide the latest information through their social media accounts. By registering or following these and checking their posts regularly, you can stay up-to-date with the latest information. It is also a good idea to check websites for official announcements and news on safety issues issued by the National Consumer Center, the National Consumer Affairs Center, and related academic societies.

Explanation

Latest news and topics from companies and media

For example, the following websites, some of which charge a fee, provide up-to-date information about product development and company initiatives in an easy-to-understand manner. In many cases, the information is linked to the publication of academic papers, and if you want to stay informed, it is recommended that you sign up for email newsletters, memberships, or follow social networking accounts. However, please be sure to thoroughly check the source of the information, as it may contain information of questionable authenticity.

[English]
-IEEE brain (https://brain.ieee.org/)
-Neuroscience News.com (https://neurosciencenews.com/)
-Science (https://www.science.org/)

[Japanese]
-Brain Tech Consortium (https://brain-tech.jp/)
-Consortium for Applied Neuroscience (https://www.-can-neuro.org/index.html)
-Forbes Japan (https://forbesjapan.com/)
-Medical AI Times (https://aitimes.media/)
-MIT Tech review (https://www.technologyreview.jp/)
-Mynavi News Business information media "TECH+" .
-Neuroscience News Summary Page (https://news.mynavi.-jp/tag/brain/)
-NeurotechJP (https://www.neurotechjp.com/jp/)

In addition, it is also effective to utilize search engine alert functions, for example, Google's alert function to set automatic delivery of news searched by keywords such as BMI, BCI, neurofeedback, and Neurotech. However, please note that gathering information from search engines may result in notification of malicious or potentially dangerous sites. Also, please note that while this method allows you to quickly search for information from a wide range of sources, there is a possibility that inaccurate or unreliable information may be detected. Please exercise caution.

Appendix 3

How to get the latest information on Neurotech

Academic Information

If you want to know more specialized information, it is recommended to read academic papers. Conversely, it is also very important to check whether information spread on websites and social media is based on academic papers or not. Recently, several news sites and social media accounts explain the latest academic papers, so it is a good idea to first come in contact with academic papers through such media. There are a vast number of papers on neuroscience, and you may feel lost. However, indicators such as whether the paper is peer-reviewed (has it been reviewed by a third party?) and how many citations it has (how many people have referenced the paper in other research) will help you select a high-quality research paper. Although this is only a guide, for your reference, we have listed some major neuroscience journals that meet these criteria. By regularly checking the websites of these journals, as well as their social media accounts, you can keep up with the latest scholarly achievements in the world.

(Examples of major journals related to the field of neuroscience)
Acta Neuropathologica / Annals of Neurology / Annual Review of Neuroscience / Brain / Brain Stimulation / Clinical Neurophysiology / Current Biology / EMBO Journal / JAMA Neurology / Journal of Neuroscience / Nature Neuroscience / Nature Review Neurology / Nature Reviews Neuroscience / NeuroImage / Neurology / Neuron / Neuroscience & Biobehavioral Reviews / Progress in Neurobiology / The Lancet Neurology / Trends in Neuroscience

Public Agency Information

• OECD (https://www.oecd.org/naec/brain-capital/)
OECD stands for Organization for Economic Co-operation and Development. It was established in 1961 to promote the improvement of economic and social welfare around the world. As such, it disseminates a wide range of information, but has a page devoted exclusively to neuroscience topics, providing a reliable and up-to-date overview of the latest topics and trends.

• IEEE（https://brain.ieee.org/）
IEEE stands for Institute of Electrical and Electronics Engineers, an academic research organization and technical standards organization in the field of engineering. It contains reliable information on engineering, computing, and technology information from around the world. "IEEE brain" is a page that provides information especially on advanced brain and neuroscience technologies.

Supplementary information

Guidebook Creation Process

The "Liberation from Biological Limitations via Physical, Cognitive and Perceptual Augmentation" (Project Manager: Ryota Kanai, Representative Organization: Advanced Telecommunications Research Institute International, hereinafter referred to as "Moonshot Kanai Project"), an R&D project under Moonshot Goal 1 of the Moonshot Research & Development Program, established the "BMI Usage Guideline Development Committee" (Issue Promoter: Ryota Kanai, Araya Co., Ltd.) in July 2021 and started its activities with the aim of developing "BMI Usage Guideline" [1]. To make the Usage Guideline more neutral, in the interest of the public, and based on scientific evidence, the committee has been working on creating its organizational structure with reference to the Minds Manual for Guideline Development 2020 ver. 3.0 [24].

Meanwhile, a survey was conducted on the sales status of Neurotech products for general consumers in Japan and abroad and whether they are accompanied by scientific evidence. The survey revealed that although the number of products is increasing, most of them have not been sufficiently verified for efficacy and safety. It also became clear that although there are scientific papers that have validated these products, there are not enough high quality papers that meet the criteria of the Minds Manual for Guideline Development 2020 ver. 3.0[24]. In other words, the necessary sources for the development of the guideline do not exist. Thus, we thought that the formulation of the BMI Usage Guideline is not appropriate at this time, and it is necessary to first conduct high-quality research to verify efficacy and safety. However, it is also necessary to inform the general public immediately about the current situation to prevent inappropriate market proliferation and health hazards. Products are increasingly being marketed without clear evidence of efficacy and safety, as well as the systems and organizations that guarantee them. Therefore, we changed the name to a guidebook and began writing it to inform the general public about the current status of Neurotech products for general consumers.

The writing process began with the establishment of General Questions (hereinafter referred to as "GQ") based on contents that the general public might have questions about based on the market research[2] and literature review, and the discussion and formulation of the answers to each GQ within the Guidebook Development Committee. Next, we carefully examined the content of the report by exchanging opinions with academic societies and government agencies in specialized fields, and by conducting a questionnaire survey of the general public, while incorporating the opinions of industry, government, academia, and the private sector. For example, GQ3, "What is neuromodulation?" was written with the guidance and advice of the members of the Subcommittee on Brain Stimulation Methods of the Japanese Society of Clinical Neurophysiology[25], which is the most knowledgeable group in Japan in this field and is engaged in academic activities and alerting the public to the issue. The Ministry of Health, Labour, and Welfare (MHLW), Surveillance Guidance and Narcotics Control Division, helped us improve the text in addition to holding opinion exchange sessions on Appendix 1, "Definition of Medical Devices and Treatment of Consumer Neurotech Products". After the tentative text was completed, we asked the general public to read this document and surveyed them to see how their awareness of Neurotech had changed before and after reading the guidebook draft, and whether they had an appropriate understanding (i.e., whether the intent of the guidebook was conveyed).

Following these processes, an external evaluation was conducted by the Guidebook External Review Board, and the text was revised based on the points raised by the board members. The revised text as a whole was reviewed from a critical perspective by the members of the Subcommittee on Brain Stimulation Methods of the Japanese Society of Clinical Neurophysiology and from a legal perspective by jurists and attorneys, and revisions were made to make the text more appropriate. After these reworkings, a second external evaluation was conducted by the Guidebook External Review Board, who verified the reliability and appropriateness of the text from an objective and neutral perspective. In addition, public comments were solicited before the guidebook was released to the public, and some of the points raised were reflected in the text[26]. All in all, the Neurotech Guidebook has been completed today with the cooperation of many experts from industry, government, academia, and the private sector, and the general public. The contents of the guidebook will be updated as necessary after its release, based on the development of future research and discussions.

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The members of the Evidence Evaluation Committee: We received various suggestions for revisions to the first draft of the guidebook.

Management of COI and how to respond when it occurs

Conflict of interest (COI) is widespread in academic and scientific publications. COI has the potential to skew several aspects of research, including how a study is designed, how data is collected, processed, and published, and who is involved in the work.
COI is briefly divided into economic COI, which is related to financial relationships and acquisition of research funds with specific companies/organizations, and COI such as academic COI (research activities and expertise) that are non-economic in nature (hereinafter referred to as "academic COI"). In addition to personal COI, financial and academic COI with educational institutions such as universities and other academic organizations such as academic societies, to which the committee members belong may also affect guidebook development. Therefore, the Guidebook Development Committee formulated a method of managing COI prior to the formulation of the guidebook in accordance with the Minds Manual for Guideline Development 2020 ver. 3.0[24] and published a guideline regarding COI[1]. Specifically, the members of the Guidebook Development Committee and Secretariat, as well as members of the Guidebook External Evaluation Committee, are obliged to clarify any COI, and are required to report their financial and academic COI for the three-year period prior to their appointment. In addition, we ask them to report the existence or non-existence of COI during the previous year, if there is any COI that exceeds the standards we have set. If it is found that there is an error in previously self-reported information, they are obliged to notify the secretariat and promptly file a revised report.
Based on the COI declarations submitted by members, we checked for conflicts of interest and, if any, evaluated whether a management plan was necessary. The declaration criteria for economic and academic COI are published on the website[1]. In addition, the contents of the declarations themselves will be made public at the same time as the guidebook is published[27]. Through these efforts, we are striving to ensure that the content of the guidebook is neutral and appropriate, and to earn the trust of society in the use of Neurotech.

Selection of External Review Board Members

The Minds Manual for Guideline Development 2020 ver. 3.0[24] recommends that an external evaluation organization including diverse experts and citizens be nominated and constituted by the committee that controls the overall guideline development. Therefore, in the development of this guidebook, we considered it essential to nominate experts who have no conflict of interest or master-disciple relationship with the Guidebook Development Committe as External Review Board members, and to receive neutral and objective evaluation from a third party. In particular, considering that this guidebook deals with consumer Neurotech, a technology that can be used by anyone and, in some cases, has the potential to affect the brain, the Committee decided that it would be appropriate to request an external evaluation by a physician or an expert who is familiar with the field of Neuroethics. The names of the External Review Board members and their areas of expertise are as follows.

Dr. Ryuma Shineha (Associate Professor, Research Center on Ethical, Legal and Social Issues, Osaka University)
Dr. Shineha specializes in the sociology of science, social theory of science and technology, and science and technology policy, and has worked to clarify and resolve issues that arise when novel technologies permeate society, not only in Ethical, Legal and Social Issues (ELSI), but also in many fields such as regenerative medicine, molecular robotics, and genome editing. In particular, he has focused on addressing issues from the perspective of science and technology governance, which involves designing a system for society to make decisions or designing specific systems. Based on these achievements, he was nominated as a member of the External Review Board by the Guidebook Development Committee. It was believed that he can give an objective evaluation on how to communicate what kind of content, when it came to educating society about the new technology of Neurotech.

Dr. Yoshiyuki Takimoto (Associate Professor / Physician, Graduate School of Medicine, University of Tokyo)
Dr. Takimoto is an expert in the field of medical ethics and ELSI, and has been serving as the Director of the Center for Patient Relations and Clinical Ethics Center at the University of Tokyo Hospital since 2013. In addition, in the "Strategic Research Program for Brain Sciences," a project by the Japan Agency for Medical Research and Development, he has been working on "research on resolving ethical, legal, and social issues in neuroscience research" , and as a result, he managed the "Intellectual Network for Human, Society, and Brain Sciences[28]" and wrote the "Ethical Guide for BMI Research[22]" . With such a wealth of experience in solving issues in the field of neuroethics, he was nominated by the Guidebook Development Committee as a member of the External Review Board because it was believed that he will be able to give an evaluation from a consumer-oriented point of view, which outlines Neurotech.

Dr. Akifumi Shimanouchi (Associate Professor, Faculty of Pharmaceutical Sciences, Hoshi University of Pharmacy and Life Sciences)
Dr. Shimanouchi specializes in ethics and has an extensive record of research on ethical, legal, and social issues that should be considered when drugs exert their effects on humans, particularly from the perspective of "drug humanism" . He is also a co-author of the "Ethics Guide for BMI Research[22]" with Dr. Takimoto, and is well versed in ELSI. He was nominated by the Guidebook Development Committee as a member of the External Review Board because the knowledge and perspectives accumulated in the field of pharmacology could be applied if society experienced a situation where Neurotech is marketed without regulation and has an effect on humans, and additionally that it is necessary to receive evaluation on the role and content of this guideline from a neutral standpoint from a field other than neuroscience.

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